

MALTA FEVER: ITS OCCURRENCE IN THE UNITED STATES ARMY, WITH A REVIEW OF THE LITERATURE.¹

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HISTORICAL. Medical officers of the English army were the first to draw attention to a disease prevailing in Malta and other Mediterranean stations possessing many of the symptoms of typhoid, but differing from that disease in important respects.

In 1816 Burnett² described very fully this disease, but regarded it as being a remittent malarial fever. This view of the character of the fever was adhered to for many years, and it was not until 1878 that the distinction was clearly drawn by medical officers of England between remittent malarial fever and Malta fever.

When first described the disease was supposed to be peculiar to the Island of Malta, hence the name "Malta fever;" but continued observation has proven that it is a widespread disease throughout tropical and subtropical regions. Thus Donaldson³ has described cases in Gibraltar, Tomaselli in Sicily, Patterson in Constantinople, Oliver⁴ along the banks of the Danube, Veale⁵ in Cyprus, Musser⁶ and Cox⁷ in Porto Rico, and Chamberlain,⁸ Curry,⁹ and Strong¹⁰ in the Philippines.

Many and various were the opinions held by observers as to the etiological factors in the production of Malta fever, and it was not until the painstaking researches of Bruce were published in 1887 that anything positive was known as to the etiology. Bruce¹¹ demonstrated the cause of the disease to be a micrococcus, to which he gave the name "micrococcus melitensis." His researches threw a flood of light upon the etiology and pathology of this hitherto obscure disease.

I shall not enter here into any detailed description of the pathology or symptomatology of Malta fever, save to say that it is generally a fever of long duration, subject to frequent relapses, presenting a most irregu-

¹ With permission of the Surgeon-General, U. S. A., from report to the Surgeon-General.

² Burnett. Practical Account of the Mediterranean Fever, London, 1816.

³ Donaldson. Army Statistical Reports, 1839.

⁴ Oliver on Danubian Fever. Lancet, 1892, vol. II. p. 1359.

⁵ Veale. Report on Cases of Fever from Cyprus, Malta, and Gibraltar. Army Medical Department Reports, England, 1879.

⁶ Musser. Philadelphia Medical Journal, December, 1898.

⁷ Cox. Report of Surgeon-General, U. S. A., 1899, p. 285.

⁸ Chamberlain. Report of Surgeon-General, U. S. A., 1900, p. 226.

⁹ Curry. Report of Surgeon-General, U. S. A., 1900, p. 226; also Journal of Medical Research, July, 1901, vol. VI. No. 1, pp. 241-248.

¹⁰ Strong's Report of the Surgeon-General, U. S. A., 1900, p. 227.

¹¹ Note on Discussion of Micro-organism in Malta Fever, Practitioner, vol. xxxiv, p. 161; also Observations on Malta Fever, British Medical Journal, May 18, 1889.

lar and confusing temperature course and accompanied by severe pain in the joints, constipation, profuse perspiration, and often followed by arthritic pains, with or without swelling of the joints. An enlarged and tender spleen is very common. The diagnosis of the disease has heretofore presented many difficulties, as it resembles in many instances typhoid or remittent malarial fever; and even with the help of the microscopic examination of the blood and the Widal test the distinction between these diseases cannot always be made. In 1897, however, Wright, of the Royal Army Medical School, England, discovered that the blood serum of a patient suffering from Malta fever will agglutinate the micrococcus melitensis in very dilute solution, and that this agglutination test is most delicate and can be depended upon absolutely in diagnosis. I will give in detail the methods of performing the test later.

DESCRIPTION OF CASES. At the United States Army General Hospital, Presidio of San Francisco, Cal., the blood of every patient admitted is examined microscopically, by order of Colonel Girard, the commanding officer. Unless specially requested by the attending surgeon, the Widal test and the agglutination test for Malta fever are not performed, so that it is possible, and indeed probable, that cases of Malta fever may have passed through the hospital without being discovered. By the courtesy of Professor Welch, Johns Hopkins University, and Professor Ophüls, Cooper Medical College, San Francisco, I have been supplied with cultures of the micrococcus melitensis, and these have been used in making the agglutination tests in the cases about to be reported.

From December 1, 1901, to date (March 24, 1902) four cases of Malta fever have come under my observation at this hospital—two during acute exacerbations of the disease and two during the chronic stage.

CASE I. *Two attacks of Malta fever, the first complicated by combined æstivo-autumnal and tertian malaria.*—This case occurred in the person of an assistant in my laboratory, who had suffered repeatedly from attacks of malarial fever, and was under the medical care of Dr. Edmund Barry, to whom I am indebted for the clinical data.

History of the Case before Admission. Name, Gustav T. W. S., private, Hospital Corps; aged twenty-eight years; birthplace, Germany. Enlisted in the United States army April 7, 1898, in New York city. He arrived in New York city from Europe in 1891, and had never been sick prior to enlistment. After enlistment he was immediately ordered to Tybee Island, Ga., where he joined Battery "F," Fifth United States Artillery. He left Tybee Island with the Battery, April 23, 1898, and was next stationed at Chickamauga Park, Tenn., where he remained one week, at the end of which time he went to Fort Tampa, Fla., and about July 1st arrived at Santiago de Cuba. He had not been sick up to this time. After the surrender of Santiago he camped until about August 15, 1898, near El Caney, and while in this camp often had slight chills, followed by a rise of temperature, and was treated with quinine. Before embarking for the United States he was stationed

for one week in the city of Santiago, doing guard duty in the streets, where he had too sleep. He left, August 23d, for the United States, and went on sick report the next day, the physician diagnosing the fever from which he was then suffering as typhoid. On September 1st he arrived at Montauk Point, Long Island, where he stayed for five days, when he was transferred to St. Catherine's Hospital, Brooklyn, N. Y. Here he improved rapidly, and about September 16, 1898, was taken as a convalescent to Shepley Hall, Atlantic Highlands, N. J., through the kindness of Miss Helen Gould. About October 4, 1898, he was granted a furlough for one month to visit Brooklyn, N. Y. The next day he was seized with a severe chill, followed by high temperature, and sent by ambulance to the Methodist Episcopal Hospital, Brooklyn, where he stayed for two weeks, after which he was transferred to St. Catherine's Hospital. At this hospital his case was diagnosed as "typhoid malaria." About December 4, 1898, he reported for duty with his Battery at Fort Hamilton, N. Y., where he stayed until March 31, 1899. During this time he had several attacks of malaria, having chills followed by fever, nausea, and vomiting, pains in all the bones, and severe headache. On April 1, 1899, he left for Manila, by way of San Francisco, and was well until July of that year, when he had slight chills at San Pedro, Macati, P. I. He also suffered from attacks during August, 1899. During January, 1890, at Bacour, P. I., he had fever and chills, with severe pains repeatedly in all the joints. He was then transferred to Manila, and while on duty at the Medical Supply Depot in that city he had several attacks of fever, with pain in all the joints, severe headache, and high temperature. In November, 1900, he was ordered to the United States, his case being diagnosed as malarial cachexia, although he had never had an examination of the blood. From November, 1900, until September, 1901, he had several chills, followed by a rise of temperature, with pain in all the bones and in the lumbar region. At this time I discovered numerous æstivo-autumnal parasites in the blood.

History of the First Attack Complicated by Malaria. On September 4, 1901, the patient had a chill, and was admitted to the hospital. At this time an examination of the blood showed a few nearly full-grown tertian parasites and numerous æstivo-autumnal parasites. Patient appeared in fairly good condition, although somewhat anæmic. He presented a coated tongue, and complained of constipation, severe headache, and backache. Physical signs negative. The case at this time was supposed to be one of malarial fever, and quinine was given in large doses. The temperature at this time did not go above 102° F., and the treatment with quinine brought it down to normal in a few days, and the patient was returned to duty. On September 18th the patient had another chill, and was again put upon sick report. An examination of the blood at this time showed a few æstivo-autumnal parasites, and treatment with quinine was resumed. Patient complained of the same symptoms as in the previous attack, but mostly of severe pains in the joints. An examination of the blood was made every day, and the æstivo-autumnal parasites disappeared by the 21st, but the patient continued to run an irregular temperature. This irregularity continued, as will be seen by reference to the chart (Chart I.), until October 13th, during which time no malarial parasites could be demonstrated in the blood, and an examination was asked for as to

the possible occurrence of Malta fever. This examination was unsatisfactory because of the fact that my culture of the micrococcus melitensis had become infected, and it was impossible to secure a new one. It was noticed, however, that a partial agglutination was obtained, and from the history of the second attack I have no hesitancy in asserting that this continuation of the temperature after heroic doses of quinine was due to the presence of Malta fever. On reference to the chart it will be seen that the temperature shows a marked quotidian character, there being a daily rise and fall, much resembling that found in many cases of tuberculosis. The highest point reached at any time was 104° F., but most of the time the temperature did not go above 102° F.

The patient gradually convalesced, and was discharged from the hospital on October 19th, after a week's normal temperature. The symptoms complained of during the time in which the malarial parasites were absent from the blood were those of pain in the joints, a feeling of marked malaise, and considerable frontal headache. Patient appeared anemic, the skin of a yellowish hue, and he became considerably emaciated. At this time he also suffered from a slight nephritis, as shown by an examination of the urine.

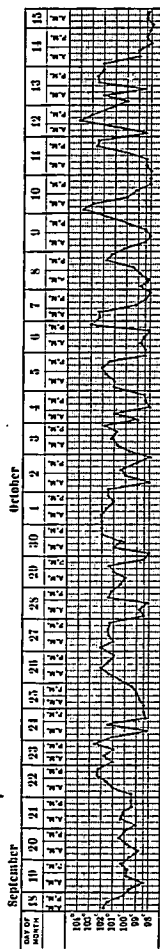
There can be no doubt, I believe, that this attack was due to Malta fever, but was complicated at its commencement by malarial fever, which soon succumbed to the influence of quinine, but which in no way affected the course of the Malta fever.

History of Second Attack. From October 19th to December 15th the patient remained comparatively well, although he complained at times of slight headache and chilly sensations, together with some pain, especially noticeable in the articulations. On the 15th of December he had a slight chill, and was readmitted to the hospital with a temperature of 100° F. An examination of his blood for ten consecutive days showed no evidence of malarial infection; but from the previous history of the case it was supposed that the temperature at this time was due to malaria, and large doses of quinine were administered. A request was not made for the Malta fever reaction until January 18th, at which time the temperature had reached normal. At this time the reaction was positive at once in a dilution as high as 1 to 250. This reaction was repeated several times, and was always found positive, and immediately cleared up the doubt which had attended the case from the commencement of the first attack.

The symptoms complained of during the second attack were similar to those of the first, there being marked pain in the joints, considerable headache, a furred tongue, and a markedly anæmic countenance. From a consideration of the chart of the second attack (Chart II.) it will be seen that the temperature during this attack differed greatly from that of the first. During the first attack the temperature was markedly quotidian in character, while during the second the temperature stayed above normal for from five to seven days at a time.

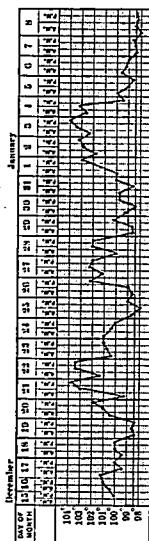
These two charts illustrate remarkably well the irregularities of the temperature in Malta fever during different attacks of the disease and of how comparatively little value the temperature chart is in these cases.

CHART I.



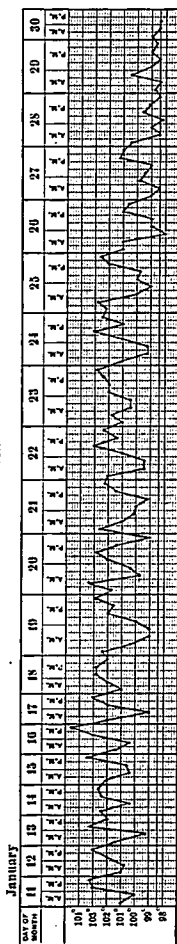
CASE I.

CHART II.



CASE I.

CHART III.



CASE II.

During the second attack the patient had no signs of nephritis, and this attack was not as severe or as long continued as the first. Patient was discharged from the hospital on January 19, 1902, having had a normal temperature for two weeks. Since that time there has been no repetition of the attacks, but he has complained considerably of stiffness in the joints and slight chilly sensations.

There can be no doubt but that this infection was contracted prior to the patient's arrival at this hospital, as he gives a distinct history of similar attacks in the Philippines, which were considered, however, of malarial character, the blood never having been examined. The occurrence of malaria, together with the first attack, further obscured the case, and led naturally to the inference that these attacks of fever were, in fact, due to malarial infection. This case shows the importance of blood examinations and the use of the agglutination test for Malta fever in the obscure fevers which are prevalent in the Orient.

CASE II.—C. H. M., musician, Company "D," Twenty-seventh Infantry, aged twenty-three years; American.

History Previous to Admission. Patient gave but little history previous to admission save that of suffering from malaria in the Philippines. He had several attacks of slight chills, followed by fever, general pain, and severe headache while campaigning, and was diagnosed as a case of malarial cachexia. He was on sick report four or five days before admission to this hospital at the Presidio, complaining of pains in the left hypochondriac region.

History after Admission. On admission patient complained of severe pain in the lumbar muscles, tenderness upon pressure over the spleen, and headache. There was considerable cough present. Bowels were constipated, and there were some mucous râles heard at the base of the right lung. The patient had an irregular temperature previous to admission, and on January 7th had a distinct chill, the temperature reaching 103° F. An examination of the blood was negative for malaria. From this time the temperature stayed above normal until January 17th, as will be seen on referring to the chart (Chart III.). On the 14th a Widal test was requested, which was negative. At this time the temperature resembled that of typhoid fever very closely, although the patient had no symptoms referable to that disease, complaining mostly of pain in the back and slight headache. Upon the 16th of January a request was made for a Malta fever test, and a reaction was obtained almost immediately with a dilution of 1:100. This test was performed repeatedly afterward until the patient's discharge from the hospital, and was always positive. Upon referring to the temperature chart in this case it will be seen that the temperature curve is irregular, the temperature from January 7th to the 17th staying above normal and resembling that of typhoid; while after the latter date the temperature became more irregular, there being a daily remission, thus approaching the quotidian character shown in Chart I. The patient ran a temperature from January 7th until January 31st, and was then returned to duty after the temperature had remained normal for several days. This infection was undoubtedly contracted in the Philippines,

as the patient had been entirely well until his arrival in the islands, and there suffered from attacks which he said were similar to the present one. The chief symptoms complained of were muscular pain, especially prominent around the articulations, and slight headache. Bowels were constipated, and considerable anæmia developed during the attack.

CASE III.—J. M., sergeant, Fourth Infantry, aged twenty-four years; American. The history of this patient previous to admission to the hospital was that of slight malarial attacks in the Philippines. On conversation with the patient he said he had suffered from several so-called malarial attacks in the Philippines, lasting from one to three weeks, although they were treated vigorously with quinine. There can be no doubt that these attacks were not malarial in character, and were probably due to Malta fever.

Upon admission to the hospital the patient appeared in good flesh, but was somewhat anæmic. He complained of constipation, there having been no bowel movements for several days. Besides constipation there was some tenderness in the region of the gall-bladder, and the patient said that he had suffered severely from muscular pain in the lumbar region and pain in the joints. Physical signs negative. Patient was admitted to the hospital January 21st, and complained of constipation. At the time of admission the temperature was 102° F., but an examination of the blood did not show any malarial infection. On January 24th a request was made for a Malta fever test, and an immediate reaction was obtained, very marked, with a dilution of 1 to 100. This reaction was repeatedly confirmed during the patient's stay in the hospital. From January 21st to the 29th the patient ran a low temperature, never above 102° F., and generally between 101° F. and normal. He complained mostly of pain in the joints. The tongue appeared fairly clean. There were no physical signs whatever which could be considered characteristic. On February 5th the patient was discharged from the hospital, having had a normal temperature since January 29th. I have not reproduced the temperature chart in this case, as it is uninteresting, showing simply a low quotidian temperature curve entirely uncharacteristic. The case is of value, however, in showing the unreliability of the temperature chart in Malta fever.

CASE IV.—N. S. L., artificer, Fourth Infantry, aged twenty-three years; American.

History Previous to Admission. Patient suffered from repeated attacks of so-called malaria in the Philippines, having chills, severe muscular pain, and headache, these attacks lasting from one to two weeks. Patient's blood was never examined, but the attacks simulated those of malaria so closely that they were considered to be of that character. Quinine was given in large doses, but had no effect on the fever.

History after Admission. Patient was admitted to this hospital January 24, 1902, with a temperature of 103° F., and complained of severe headache, backache, and pain over the spleen upon pressure. There was a history of a decided chill. He appeared anæmic and jaundiced, and was constipated, and said that he had had similar attacks in the Philippines. An examination of the blood on the 25th was negative for malaria, but gave a marked reaction with the micrococcus melitensis in a dilution of 1:100. Patient's temperature reached normal on the 26th, although no quinine had been given, and remained normal

until February 4th, at which time the patient had a slight chill, the temperature reaching 103° F., and showing a quotidian character for a period of five days after. It remained normal until he was discharged, on the 19th. During this time the patient did not appear to be very sick, the only thing complained of being pains in the joints. The temperature chart is not reproduced, as it is not of special interest.

In considering the four cases noted it will be seen that the first two cases are those of acute exacerbations of Malta fever, in which the patient runs a temperature for a considerable length of time, while the latter two cases are characteristic of the chronic form of the disease, in which the temperature is but little above normal, and the chief symptoms present are those of articular rheumatism. Both of the latter cases would have been diagnosed as cases of articular rheumatism had it not been for the Malta fever reaction.

METHODS OF PERFORMING SERUM TESTS FOR MALTA FEVER.

The serum test for Malta fever was first described by Wright, of the Royal Army Medical School, at Netley. The methods of performing the test vary somewhat, but the principle is the same in all. He discovered that the serum of Malta fever cases had the power of agglutinating the micrococcus in suspension, and that this reaction took place earlier than the Widal reaction and in much more dilute solution.

Wright's Method. Sedimentation tubes having a diameter of less than 1 millimetre and an agar culture of the micrococcus are used in making the test. A salt solution suspension is made, and this solution is used to dilute the blood serum, the dilution varying according as the test is desired to be more or less delicate. It makes no difference whether the micrococci are alive or dead, the agglutination reaction taking place as well with one as the other.

Curry's Method. Curry's method of performing the test¹ differs somewhat from that of Wright, and is thus described by him: "I used common glass tubing about 3 to 4 mm. in diameter, and made the observations macroscopically, and as a control made microscopic observations of drops of the fluid withdrawn by means of a platinum loop from the top, middle, and bottom of the tube. Tubes 7.5 cm. long and 3 to 4 mm. in diameter were made from glass tubing, and the bottoms were drawn out to a long, sharp point. These were sterilized and plugged with cotton in the dry sterilizer. Salt solution suspensions were made according to the method used by Wright. Bacteria were killed by heat at 60° C. for fifteen minutes, and 0.5 per cent. carbolic acid added. As a routine method one drop of blood serum was mixed with nineteen drops of normal salt solution, then equal parts of this mixed with the salt suspension of the culture of the micrococcus *melitensis* and placed in the small tubes of the sterile pipette. This equals

¹ "Malta Fever," Journal of Medical Research, vol. vi., No. 1.

a dilution of 1 to 40. A reaction was called positive and complete only when, in addition to the precipitation of the bacteria in the bottom of the tube, the supernatant fluid became clear.

Author's Method. In performing the serum test for Malta fever I have used practically the same method as that used for making the Widal test. A pure culture of the micrococcus, either upon agar or in bouillon, was used. The test may be performed either with the fresh serum or with a dry drop of blood, the latter being used preferably, as it is simpler and easier to procure. A drop of blood is secured upon a glass slide and diluted with enough sterilized water to dissolve it. A graduated pipette of very small calibre is used to make the dilution with the micrococcus. Having dissolved the drop of blood, a known portion is taken from it by the pipette and placed upon a clean slide; this is then diluted with a measured quantity of the bouillon culture or with a suspension of the agar culture made with sterilized water. The pipette is so graduated that a dilution can be made from 1:10 to 1:150. A cover-glass is then placed over the mixture, and this examined microscopically. In using the agar suspension the drop should first be examined so as to be sure there is no agglutination present before the blood is added. Preferably I have used a dilution of 1:75, although the agglutination reaction has been obtained with dilutions as high as 1:250 immediately. This method is easy of performance, all that is needed being the culture, the special graduated pipette, the cover-glass and slides, and the drop of blood. The method was used in all the cases described, and controls with a serum of other diseases—such as typhoid, dysentery, etc.—made at the same time, and it was found perfectly reliable.

LITERATURE. The literature concerning the appearance of Malta fever among the soldiers of the United States army is very limited. The first case described was that of Dr. Musser, of Philadelphia, in the *Philadelphia Medical Journal* December, 1898. His case was that of an officer who contracted the disease in Porto Rico, and he was the first to draw attention to the fact that the disease was probably endemic in that island.

In the *Report of the Surgeon-General of the Army for 1899*, Walter Cox described a case occurring in Porto Rico and observed by him. The patient was a private of the Hospital Corps, aged thirty years. He came under observation January 14, 1899. He contracted fever in the guard-house of an old Spanish barracks, the fever commencing January 11, 1899. He complained of pain all over the body, especially in the bones and joints. Had two chills on successive days, but none afterward. This was at the commencement of the illness. The appetite was poor, and the bowels were at first loose and later constipated. The temperature curve showed daily remissions and reached normal

gradually. The morning temperature for a considerable time reached the normal point, but was 1, 2, or 3 degrees above normal toward evening. He was discharged from the hospital on April 3d, after about a week of normal temperature, but was readmitted April 7th, suffering again from fever. This attack was similar to the first. The blood was examined repeatedly for the malarial parasites as well as for the Widal reaction. A test with a culture of the micrococcus melitensis showed a marked agglutination in dilutions as high as 1:60.

Chamberlain, while on duty on the hospital ship "Relief," at Manila, P. I., observed two cases of the disease in soldiers, which were reported to the Surgeon-General of the Army. The men were in adjacent beds, and both presented mild attacks. The temperature curve was irregular, being neither markedly remittent nor undulating. The cases were first diagnosed as malarial fever, but the Malta fever reaction was performed at the laboratory of the First Reserve Hospital, and both were found positive. Examination of the blood for malarial parasites and the use of the Widal test both resulted negatively.

Curry and Strong, in 1900, reported cases occurring at the First Reserve Hospital. Strong performed an autopsy upon a man who had died from a continued fever of long duration. The post-mortem showed that it was neither typhoid nor malaria, and cultures from the case made by Curry resulted in the finding of the micrococcus melitensis. Inoculations into monkeys produced the typical symptoms of Malta fever. While performing these experiments Strong became infected and suffered from a typical attack of the fever. In another case the condition was discovered post-mortem, and cultures were obtained of the micro-organism. At this time two cases were observed in the wards of the hospital which gave the reaction with the micrococcus, and were undoubtedly cases of Malta fever.

The most valuable report of Malta fever occurring in soldiers of the army is that written by Curry and published in the *Journal of Medical Research*, vol. vi., No. 1. In this report Curry describes the cases which have come under his observation both in Manila and in the Army and Navy General Hospital, at Hot Springs, Ark. Besides the four cases of Malta fever observed in Manila, he observed in all eight cases of Malta fever in the hospital at Hot Springs. Four of these are described *in extenso*, the notes of the other four cases occurring in a note at the end of the report. All four of the latter cases were in a convalescent stage, the prominent symptoms being those of articular rheumatism, constipation, and frequent profuse sweatings. These cases were all diagnosed as articular rheumatism. Of the four cases described more fully all gave a marked serum reaction with the micrococcus melitensis when in a dilution as high as 1 to 300. None of the cases presented the symptoms found in the acute stage. The

symptoms complained of were pain in the articulations, constipation, and sweating, and all showed anæmia. These cases were all supposed to be suffering from chronic articular rheumatism.

In his recapitulation Curry says: "We have four cases of what was thought on admission to be chronic rheumatism. These cases have not improved under treatment nor by change to this favorable climate. Neither antirheumatic nor antimalarial treatment has benefited these men. In spite of treatment and favorable conditions, repeated and more or less regular recurrences of acute rheumatic pains and swellings and of fever have taken place. These conditions have lasted a long time—from six months, the shortest, to sixteen months, the longest of the series. The other prominent symptoms have been anæmia, profuse sweatings, and constipation. The blood examinations for malarial fever and for typhoid were negative, save in the case of one who had had severe typhoid fever two years ago. The clinical history of these cases corresponds with that of Malta fever, and the result of the serum test with the micrococcus makes it certain that the diagnosis of Malta fever in these cases is a correct one."

The important lesson to be learned from a study of the literature of Malta fever occurring in the United States army, and from the study of the cases described in this report, is that the condition is one not easily recognized clinically, and one apt to be mistaken for typhoid, malaria, or, in the chronic stage, for articular rheumatism. This being so, the great value of a microscopic examination of the blood and the performance of the serum test is at once proven. None of the cases observed by me was diagnosed as Malta fever, and in only one of them was there any suspicion of the occurrence of this disease. The two cases presenting the chronic symptoms would, in all probability, have been transferred to Hot Springs, Ark., for antirheumatic treatment, while in the two cases presenting the acute symptoms the patient would probably have been treated for either malaria or typhoid fever. In fact, in Case I, on account of finding malarial parasites at different times in the patient's blood, the treatment had been altogether that for malaria; and had a diagnosis of Malta fever been made more quickly much discomfort would probably have been saved the patient. The following conclusions may be drawn from the study of these cases:

1. There occurs in the tropics and subtropics a fever which may resemble in its acute stage either typhoid or malaria, and in its chronic stage articular rheumatism, caused by the micrococcus *melitensis*.

2. There are no pathognomonic symptoms of Malta fever. The symptoms observed are so inconstant and confusing that no one of them can be said to be typical of the disease.

3. A differential diagnosis of this fever is almost impossible in the majority of cases without the aid of the microscope and the serum test.